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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,428	04/06/2001	Seth J. Orlow	71369.162	6098

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EXAMINER

COOK, REBECCA

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 09/11/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/827,428

Applicant(s)

ORLOW ET AL.

Examiner

Rebecca Cook

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 70-82,91 and 92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 70-82, 91-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14,16. 6) ☐ Other: _____

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Upon reconsideration the election requirement of 22/27/02 has been withdrawn. Claims 70-82, 91-92 will be examined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 70-82, 91-92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not provide examples of art recognized assays that are useful to identify compounds useful in a composition to reduce skin pigmentation by effecting an alteration in late endosomal/lysosomal trafficking in a skin cell; and to identify compounds that modulate melanogenesis by affecting P protein function, that inhibit late endosomal/lysosomal trafficking or inhibit an ATPase.

Claims 70-82, 91-92 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for any and all intended compounds of the composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400)

- 1) Nature of invention.

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- 2) State of prior art.
- 3) Level of ordinary skill in the art.
- 4) Level of predictability in the art.
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention

based on the content of the disclosure.

1) Nature of the invention.

Claims 70-82 are drawn to a pharmaceutical composition for reducing skin pigmentation comprising a compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell. Claims 91-92 are drawn to a kit comprising a compound that modulates melanogenesis by affecting P protein function, inhibiting late endosomal/lysosomal trafficking or inhibiting an ATPase. The compounds in the compositions of the kit can either reduce or increase skin pigmentation.

2) State of the prior art.

The references do not indicate which compounds may be useful in the claimed inventions.

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. The composition and kit encompass a vast number of compounds. Applicant's specification does not enable the public to identify such a numerous amount of compounds.

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4) Level of predictability in the art.

The art pertaining to the identifying compounds that reducing skin pigmentation comprising a compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell, modulates melanogenesis by affecting P protein function, inhibiting late endosomal/lysosomal trafficking or inhibiting an ATPase is highly unpredictable.

5) Amount of direction and guidance provided by the inventor.

The compound that provides the desired skin pigmentation effects encompasses a vast number of compounds. Applicant's disclosure on page 42 provides no guidance on a test that would screen for compounds that effect an alteration in late endosomal/lysosomal trafficking and does not enable the public to identify or prepare said compounds. While applicants have generally described characteristics to measure for to identify compounds that modulate melanogenesis by affecting P protein function, they do not disclose any specific art recognized assays. No guidance is provided for a test that would screen for compounds that inhibit an ATPase.

It is noted that a number of assays would be required. One would be to identify compounds useful in a composition to reduce skin pigmentation by effecting an alteration in late endosomal/lysosomal trafficking in a skin cell. The second would be to identify compounds that increase melanogenesis by affecting P protein function. The third would be to identify compounds that decrease melanogenesis by affecting P protein function. The fourth would be to identify compounds that increase melanogenesis by inhibiting an alteration in late

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endosomal/lysosomal trafficking in a skin cell. The fifth would be to identify compounds that decrease melanogenesis by inhibiting late endosomal/lysosomal trafficking in a skin cell. The sixth would be to identify compounds that increase melanogenesis by inhibiting an ATPase. The seventh would be to identify compounds that increase melanogenesis by inhibiting an ATPase.

6) Existence of working examples.

No working examples of specific intended compositions are provided.

7) Breadth of claims.

The claims are extremely broad due to the vast number of possible compounds for the composition of claim 70 and the kit of claim 91.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with this claim. In particular, the specification fails to enable the skilled artisan to practice the invention without undue experimentation. The skilled artisan would have to perform an indefinite amount testing in order to obtain compounds useful in the claimed composition and kit. Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not perform the claimed process without undue experimentation, see *In re Armbruster* 185 USPQ 152 CCPA 1975.

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Furthermore, MEDLINE AN 67014260 and MEDLINEAN 89379530 disclose that chlorpromazine, a phenothiazine compound intended for use in the instant inventions, produces skin pigmentation.

Applicants' argument that the amended claims are directed to compositions formulated for topical compositions, while the references do not teach that chlorpromazine would cause skin pigmentation when applied topically, is not persuasive. Once absorbed through the skin the compound would be expected to produce the same effect that it does when taken orally.

Claims 70-82 and 91-92 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 70-82 it is still confusing whether the word "alteration" is intended to inhibit or activate late endosomal/lysosomal trafficking. Applicants' argument that the claims recite compounds that reduce skin pigmentation is not persuasive in view of their argument that the term "modulate" encompasses compounds that both decrease and increase skin pigmentation. It would be obvious to one of ordinary skill in the art that the word "alteration" would also apply to compounds that both decrease and increase skin pigmentation, since "alter" and "modulate" are both defined in Webster's II, New Riverside University Dictionary, 1984 as "adjust."

In claims 91-92 the phrase "modulates melanogenesis" is still confusing. It is not clear how inhibiting late endosomal/lysosomal trafficking and inhibiting an

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ATPase can both decrease skin pigmentation and increase skin pigmentation and applicants have not clarified this.

In view of applicants' arguments the remaining earlier rejections under 35 U.S.C. 112, paragraph two to claims 70-73 and 75 are withdrawn.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 70-73 are rejected under 35 U.S.C. 102(b) as being anticipated by CA126:190762. The reference discloses a compound of formula I that corresponds to compound (d) of instant claim 73 and that it is used in topical preparations. Applicants' argument that CA126:190762 does not disclose a topical composition that includes a skin pigmentation reducing effective amount of a compound that effects an alteration in late endosomal/lysosomal trafficking in a skin cell has been considered but are not persuasive, since intended use is not patentable in a composition claim.

Claims 70-73 and 81 are rejected under 35 U.S.C. 102(a) as being anticipated by CA129:347178. CA129:347178 (abstract, lines 1-2) discloses a composition for topical use comprising a sphingosine. The claims appear to differ over CA129:347178 in reciting a compound that reduces skin pigmentation

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by affecting an alteration in late endosomal/lysosomal trafficking in a skin cell.

However, intended use does not impart patentability in a composition.

Claims 70-73, 75-78 are rejected under 35 U.S.C. 102(b) as being anticipated by CA50:17370. CA50:17370 (abstract, lines 1-3) discloses a composition for topical use comprising chlorpromazine. The claims appear to differ over CA50:17370 in reciting a compound that reduces skin pigmentation by affecting an alteration in late endosomal/lysosomal trafficking in a skin cell.

However, intended use does not impart patentability in a composition.

Claims 70-74 are rejected under 35 U.S.C. 102(a) as being anticipated by CA129:184644. CA129:184644 (abstract, lines 4-6) discloses a composition for topical use comprising progesterone. The claims appear to differ over CA129:184644 in reciting a compound that reduces skin pigmentation by affecting an alteration in late endosomal/lysosomal trafficking in a skin cell.

However, intended use does not impart patentability in a composition.

Claims 70-73, 75-76 and 79-80 are rejected under 35 U.S.C. 102(b) as being anticipated by MEDLINE AN 1998010047. MEDLINE AN 1998010047 ((abstract, line 4) discloses a composition for topical use comprising progesterone. The claims appear to differ over MEDLINE AN 1998010047 in reciting a compound that reduces skin pigmentation by affecting an alteration in late endosomal/lysosomal trafficking in a skin cell. However, intended use does not impart patentability in a composition.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 70-73, 82 rejected under 35 U.S.C. 103(a) as being unpatentable over 3,389,051 (Kagan) in view of CA117:239546. Kagan (column 1, lines 23-33, column 4, lines 70-75) discloses a compound of formula I which corresponds to compound VIII of instant claim 82 and its use in a composition. The instant claims differ over Kagan in reciting a compound that reduces skin pigmentation by affecting an alteration in late endosomal/lysosomal trafficking in a skin cell and its use in a topical formulation. However, intended use does not impart patentability in a composition. Furthermore, Kagan (column 4, lines 70-75) discloses that the compositions can be adapted for use in suitable forms. It would be obvious to one of ordinary skill in the art to deliver the composition of Kagan in a topically applied, controlled-release delivery system disclosed by CA117:239545, since said topically applied, controlled-release delivery system for drugs is a convenient, suitable method to deliver a drug.

Claims 91-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over CA126:190762 (abstract, lines 1-5, compound I). CA126:190762 (abstract, compound I) discloses a compound that inhibits melanin formation and that it may be used in a topical composition. Said compound corresponds to a compound disclosed in the specification that effects the alteration in late endosomal/lysosomal trafficking. The instant claims recite a kit comprising a compound that modulates melanogenesis by recited mechanisms of action and

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that it further may contain a set of written instructions. Applicants' argument that CA126:190762 would not modulate melanogenesis by the mechanisms recited in claim 91 is not persuasive, since intended use does not impart patentability to a composition claim. Furthermore, no unobviousness is seen in applicants' nominal recitation of instructions for use, since the printed matter would not present any unusual and/or unexpected requirement apart from conventional and well-known procedures. The inclusion of a package insert including written instructions describing how to use a composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art. It is well settled that in the absence of some distinguishing procedure or step, instructions cannot be relied upon to impart patentability over well-known pharmaceutical formulations.

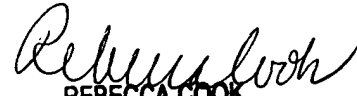
In view of the amendments to the claims the rejections under 35 USC 102 and 103(a) over CA130:295103 and EMBASE 1998386460 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cook whose telephone number is (703) 308-4724. The examiner can normally be reached on Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


REBECCA COOK
PRIMARY EXAMINER
GROUP 1200/614

September 10, 2003